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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,534	01/16/2001	Qian Huang	0399.2006-003	5869

21005 7590 12/17/2003

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/17/2003

26

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,534	HUANG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *36-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06/052003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18*.
4) ☒ Interview Summary (PTO-413) Paper No(s). *19*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 36-86 are pending.

Response to Amendment

This is a response to the amendment, paper No. 15, filed 06/05/03. Claims 1-35 have been canceled. New Claims 36-86 are added. Claims 36-86 are pending before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New matter objection

The amendment filed 06/05/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the recitation of "a homolog thereof" in line 3 of claims 36 and 53, the recitation of " homolog" in line 1 of claims 39, 40, 43, 54, 55, 58, 73, 74, 77 and "a homolog thereof" in line 4 of claim 68.

Applicants as the support of the amendment have been reviewed. They are all directed to the Hsp ATP minding domain. However, there is no teaching about a homolog thereof of SEQ ID NO: 8. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, ¶ 2

Because claims 25-35 are canceled and new claims 36-86 are added. The rejections of claims 26-35 under ***35 USC § 112*** is moot in view of the new ground rejection.

Claim Rejections - 35 USC § 112 ¶ 1

Because claims 25-35 are canceled and new claims 36-86 are added. The rejections of claims 26-35 under ***35 USC § 112*** is moot in view of the new ground rejection.

Double Patenting

Because Applicants cancel the claims 26-31 and 35, The Double patenting issue over claims 26-31 and 35 are moot in view of the new ground of the rejections.

New grounds of Rejections:

New Matter Rejections

1. Claims 36, 53, 39, 40, 43, 54, 55, 58, 68, 73, 74 and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the added material which is not supported by the original disclosure is as follows: the recitation of "a homolog thereof" in line 3 of claims 36, 53, the recitation of " homolog" in line 1 of claims 39, 40, 43, 54, 55, 58, 73, 74, 77 and "a homolog thereof" in line 4 of claim 68.

2. Applicants as the support of the amendment have been reviewed. They are all directed to the Hsp ATP minding domain. However, there is no teaching about a homolog thereof of SEQ ID NO: 8. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, ¶ 2

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 36-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 36, 39, 40, 43, 53, 54, 55, 58, 68, 73, 74 and 77 are vague and indefinite in that the metes and bounds of "homolog" are not defined. The claims are interpreted in light of the specification; however, the specification does not give the definition of "homolog". Moreover, Applicants are reminded that in the art, identity, homology or sequence similarity can be calculated by a variety of different methods, whereby the calculated identity between two

sequences will be quite different depending on the algorithm used for calculation. For example, the calculation of "identity" is affected by variables such as the relative weight given to the sequence gaps versus mismatches, or whether conservative substitutions are weighted differently from non-conservative substitutions. This rejection affects the dependent claims 37-38, 41-42, 44-52, 56-57. 59-67, 69-72, 75-76 and 78-86.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 68-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

7. In the instant case, the specification do not have a position of any composition comprising a portion of Hsp having at least 50% or 1-25, or 10-14% or 10-20% of amino acid residues substitution of SEQ ID NO: 8.

8. In response to the Office Action, Applicants amend the claims 36 and 86 as SEQ ID NO: 8 and homolog thereof and argue that one ordinary skill in the art would recognize that Applicants were in the possession of SEQ ID NO: 8, as well as the claims variants thereof.

9. Applicants' argument has been respectfully considered; however, it is not found persuasive because Applicants do not have a disclosure that supports the broadly claimed Hsp fragment read on any hsp fusion polypeptide comprising 1-25% or 10-20% or 50% amino acid substitution of SEQ ID NO: 8.

10. 35 USC 112 requires inter alia that "a patent specification contain a written description of the invention and the manner and process of making and using it in such full clear and concise terms as to enable one skilled in the art to make and use the invention". Applicants also reminded that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled

chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 36-40, 44-46, 50-51, 59-61, 65-67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-52 of U.S. Patent No. 6,338,952 in view of Siegel et al. (US Patent No. 6,495,347).

13. Claimed invention is drawn to a composition comprising a portion of Hsp 70 of SEQ ID NO: 8 or homolog thereof, joined with a heterologous viral antigen vial peptide bound, such as HIVp214, gp41 or HPV E17. The composition further comprises a pharmaceutical acceptable surfactant, an excipient, a carrier or a diluent.

14. Claims 43-52 of Young's patent disclose a pharmaceutical composition comprising a fusion protein comprising a portion of a mycobacterial heat shock protein Hsp70 joined to a viral antigen via a peptide bound, wherein the composition further comprises a pharmaceutically acceptable carrier or excipient. The viral antigen is HIV p24 protein or peptide antigen. Young

does not teach that the portion of the Hsp70 is a fragment of Hsp70 limited to SEQ ID NO: 8 or homolog thereof. Young particularly point out that mycrobacterial stress protein (synonym of Hsp) is among the immunodominant target of both antibody response and T cell response. Any stress-induced protein or other functional equivalences can be used any stress-induced protein by their invented method for producing an enhanced immune response against an infection by a pathogen (See line 53 on col. 5 through line 39 on col. 10).

15. Siegel et al. disclose a composition and a method of using the composition to induce Th1 like immune response, wherein the composition comprising a fusion protein made from the conjugated Hsp65, 40, 10, 60 and 71 with a heterologous sequence encoding human viral antigenic polypeptide, such as HPV, HSV, HCV, HBV, CMV and EBV. In particular, Siegel et al. use a portion of M Tuberculosis Hsp of SEQ ID NO: 41 or SEQ ID NO: 45, which have more than 99% homology to the portion of M Tuberculosis Hsp of SEQ ID NO: 8 of current application. The Hsp of SEQ ID NO: 41 or 45 is covalently linked to a heterologous sequence encoding a viral antigen, especially HPV E7. The administration of the composition comprising the portion of M. Tuberculosis Hsp conjugated with HPV E17 antigen induces an enhanced Th1 like immune response (See lines 8-21 on col. 2 and examples 14-22 on col. 21-28). The Th1 like immune response is directed to a Th1 cells participated cell mediated immune response by producing lymphokine, such as INF-λ and TNF-β (See lines 28-32 on col. 1). It is well known I the art that the activated CD8+ T cells secret INF-λ and the INF-λ in return activates the T-cell mediated immune response including the CD8+ T lymphocyte cytotoxic immune response.

16. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Young and further in view of the disclosure of Siegel et al. to make immunogenic composition comprising a portion of Hsp70, SEQ ID NO: 8 homolog and conjugate it with any viral antigen to induce an enhanced CD8+ T cell mediated CTL immune response absence of unexpected results because Yung already discloses that Hsp70 family fusion proteins are generally useful as an immunogens for stimulating CD8+ CTL and Siegel et al particularly demonstrate a portion of Hsp70, which is a homolog of SEQ ID NO: 8 is suitable for conjugating a viral antigen to produce an enhanced Th1 type immune response, including $CD8^+$ CTL response absence of unpredicted result.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

17. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. Claims 36-39, 43-46, 53-54, 59-61, 68-73 and 77-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Siegel et al. (US Patent No. 6,495,347B1).

19. Siegel et al. disclose a composition and a method of using the composition to induce Th1 like immune response, wherein the composition comprising a fusion protein made from the conjugated Hsp65, 40, 10, 60 and 71 with a heterologous sequence encoding human viral antigenic polypeptide, such as HPV, HSV, HCV, HBV, CMV and EBV. In particular, Siegel et al. use a portion of M Tuberculosis Hsp of SEQ ID NO: 41 or SEQ ID NO: 45, which have more than 99% homology to the portion of M Tuberculosis Hsp of SEQ ID NO: 8 of current application. The Hsp of SEQ ID NO: 41 or 45 is covalently linked to a heterologous sequence encoding a viral antigen, especially HPV E7. The administration of the composition comprising the portion of M. Tuberculosis Hsp conjugated with HPV E17 antigen induces an enhanced Th1 like immune response (See lines 8-21 on col. 2 and examples 14-22 on col. 21-28). The Th1 like immune response is directed to a Th1 cells participated cell mediated immune response by producing lymphokine, such as INF-λ and TNF-β (See lines 28-32 on col. 1). It is well known I the art that the activated CD8+ T cells secret INF-λ and the INF-λ in return activates the T-cell mediated immune response including the CD8+ T lymphocyte cytotoxic immune response. Siegel et al. also disclose that the Hsp can be any polypeptide consisting of a sequence that is at

least eight amino acids in length of a fragment thereof. The Hsp polypeptide refers to a polypeptide consisting of a sequence that is at least 40% identical to that of a Hsp. Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 63-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young (WO 98/35705A1) and Siegel et al. (US Patent No. 6,495,347B1).

21. Young disclose a recombinant fusion protein made by hsp 70 of M. tuberculosis or a heat shock protein selected from nonhuman mammalian heat shock proteins, insect heat shock protein and fugal heat shock protein and mammalian heat shock protein, which is suitable for conjugating or joining with other moiety, such as protein, peptide, lipid, carbohydrate, glycoprotein, and/or small organic molecule, including functional enzyme, hormone, protease, toxin, toxoid and/or cytokine to enter the cell and play a biological function (See lines 25 on page 7 to line 9 on page 8 and claims 1-4). In particular, Young demonstrates that a recombinant M. Tuberculosis hsp70 protein was purified according to the method disclosed by Suzue K et al.(J. Immunol. 1996, Vol. 156, pp. 873-879) and utilized to elicit MHC class-I restricted CD8+ CTL (See lines 10-19 on page 9 and lines 23-25 on page 21). While Young does not particularly teach to use Hsp of SEQ ID NO: 8, the SEQ ID NO: 8 of the Hsp of current Application is a fragment of M. tuberculosis Hsp70 disclosed by Young. Especially, Young further teach that the term of "Hsp" also includes a protein having an amino acid sequence, which is the functional equivalent of Hsp in that it is sufficient homologous in amino acid sequence to that of the Hsp to be capable of delivering or chaperoning the carried a moiety to entry into a cell, wherein the moiety does not enter cells on its own. The term " sufficient homologous in amino acid sequence to that of the Hsp means that the amino acid sequence of the protein or polypeptide will

generally show at least 40% to 95% identity with the Hsp amino acid sequence (See lines 6-24 on page 7). Yung also discloses that Hsp70 fusion proteins are generally useful as an immunogens for stimulating CD8+ CTL.

22. Siegel et al. disclose a composition and a method of using the composition to induce Th1 like immune response, wherein the composition comprising a fusion protein made from the Hsp65, 40, 10, 60 and 71 conjugated with a heterologous sequence encoding human viral antigenic polypeptide, such as HPV, HSV, HCV, HBV, CMV and EBV. In particular, Siegel et al. use a portion of M Tuberculosis Hsp of SEQ ID NO: 41 or SEQ ID NO: 45, which have more than 99% homology to the portion of M Tuberculosis Hsp of SEQ ID NO: 8 of current application. The Hsp of SEQ ID NO: 41 or 45 is covalently linked to a heterologous sequence encoding a viral antigen, especially HPV E7. The administration of the composition comprising the portion of M. Tuberculosis Hsp conjugated with HPV E17 antigen induces an enhanced Th1 like immune response (See lines 8-21 on col. 2 and examples 14-22 on col. 21-28). The Th1 like immune response is directed to a Th1 cells participated cell mediated immune response by producing lymphokine, such as INF-λ and TNF-β (See lines 28-32 on col. 1). It is well known I the art that the activated CD8+ T cells secret INF-λ and the INF-λ in return activates the T-cell mediated immune response including the CD8+ T lymphocyte cytotoxic immune response.

23. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Young and further in view of the disclosure of Siegel et al. to make immunogenic composition comprising a Hsp70 fusion protein, such as the Hsp homologous protein of SEQ ID NO: 8 homolog that is conjugated with any viral antigen or bacterial antigen as well as biologically active moiety including toxin or glycoprotein as taught by Young and use the composition to induce an enhanced CD8+ T cell mediated CTL immune response absence of unexpected results because Yung already discloses that Hsp70 family fusion proteins are generally useful as an immunogens for stimulating CD8+ CTL and Siegel et al particularly demonstrate that Hsp that is s homolog of SEQ ID NO: 8 is suitable for conjugating a viral antigen for producing an enhanced Th1 type immune response, including $CD8^+$ CTL response.

24. As there are no unexpected results have been provided, hence the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

2. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

4. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

5. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
November 17, 2003

JAMES HOUSEL 12/15/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600